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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/677,777	TOVEY	
	Examiner	Art Unit	
	Laura M. Mitchell	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *35-69* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34 and 70-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

It is noted that claims 1-29, 32, 34-38, 42-44, 46, 49, 50, 53, 58, 61-63 and 66 have been amended, claims 35-69 are withdrawn and claims 70-75 have been added in the amendment filed 12/5/2006. Claims 1-34 and 70-75 are under examination.

It is noted that claim 34 was previously indicated as allowable, however after further consideration new grounds of rejection have been applied below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-34 and 70-75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claim 1 is drawn to a cell line transformed with a reporter gene construct with the property that it will maintain signal transduction activity for at least an hour no more than about 30 days at a temperature above freezing. Claim 2 is drawn to the cell line of claim 1 in a frozen state. Claims 1-2 have been amended to recite the additional limitation that the cell line "will lose said signal transduction activity and undergo cellular death in no more than about 30 days at a temperature above freezing".

New claim 70 is drawn to a cell line of claim 1, wherein the cell will undergo cellular death in no more than about 24 hours at a temperature above freezing. New claim 71 is drawn to a cell line of claim 1, wherein the cell will undergo cellular death in no more than 14 days at a temperature above freezing.

Claims 1-2 are drawn to cell lines and do not recite that the cell lines have been treated in any manner that would convey the property of "cellular death in no more than about 30 days". The specification does not disclose an untreated cell line with this property. Claims 70-71 are drawn to cell lines and do not recite that the cell lines have been treated in any manner that would convey the property of "cellular death in no more than about 14 days" or "no more than about 24 hours". The only disclosure of cells with these properties is cell lines that have been treated with γ-radiation or with an anti-mitotic and pro-apoptotic agent. The specification only discloses cell lines that have been treated with an anti-mitotic and pro-apoptotic agent that would have the property of a predicable cellular death. Therefore, amended claim 1-2 and new claims 70-71 constitute **impermissible new matter**.

The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention.

Furthermore, Applicants claim a cell line comprising a reporter gene construct comprising a reporter gene operatively linked to one or more transcriptional control elements that are regulated by the signal transduction activity of a cell surface protein in response to an extracellular signal, and wherein the cell line has been treated with an anti-mitotic and pro-apoptotic agent and then has been resuspended in a cryopreservative such that the cell maintains signal transduction activity and undergoes cellular death in no more than about 30 days at a temperature above freezing, in no more than about 14 days (claim 71) or in no more than about 24 hours (claim 70). As written, the claims have not established a structure function relationship between the anti-mitotic and pro-apoptotic agent and maintenance of the signal transduction activity for a particular time and cellular death after a particular time period.

The specification discloses that the cell line can be any prokaryotic or eukaryotic cell, which is a very broad genus of cells (see paragraph 0067). The specification discloses that there are multiple classes of cell surface receptors and corresponding extracellular signals, including interferon receptors, cytokine receptors, G-coupled receptors and growth factor receptors, for example (see paragraph 0009-0024). Therefore, the claims encompass a very large genus of cell surface proteins and signals to regulate signal transduction activity. The specification discloses transcriptional control elements, including preferred embodiments of an interferon stimulatory response element (ISRE) and/or a gamma activated sequence (GAS). In the instant case, the specification discloses a human promonocytic cell line (U937 or PIL5) for the claimed cell line. The cell line has been transformed with constructs comprising ISRE-SV40 operably linked to reporter gene and responsive to interferons I or II. The specification discloses treatment of cell lines with anti-mitotic and pro-apoptotic agents such as 5-fluorourcil, vinblastine or γ- radiation. The claims do not establish a relationship between treatment with said agent and ability to maintain signal transduction activity for a specific period of time. The specification discloses that an anti-mitotic and pro-apoptotic agent will affect a treated cell when it begins to replicate by inducing apoptosis. The specification also discloses that high doses of radiation will cause a cell to lose its signal transduction activity, and that low doses of irradiation will cause a cell to cease replication and undergo cell death. Therefore the limitations of how long the claimed cell line will maintain any particular signal transduction activity for the claimed time of at least about 1 hour depends on its reaction to low dose radiation, or the claimed agents. In addition, the characteristics of the claimed cell line regarding a time period after which when signal transduction activity will be lost and the cell will die appears to be dependent on the length of the replication cycle since the anti-mitotic and pro-apoptotic agent would only be effective on the start of replication. The specification contemplates any eukaryotic or prokaryotic cell, but does not describe the replication cycle times of even a few of the cells. Furthermore, the specification exemplifies cell lines treated with anti-mitotic and pro-apoptotic agents such as 5-fluorourcil, vinblastine or γ-radiation, but does not describe any other anti-mitotic and pro-apoptotic agent.

There is no description of any other cell lines which have been transformed with any other reporter gene construct comprising particular transcription control elements regulated by any other cell surface proteins. There is no description of any other cell line that has been treated with any other anti-mitotic and pro-apoptotic agent. Since the time after which the cell line would undergo cell death is dependent on the cell cycle of any particular cell type and the activity of the anti-mitotic and pro-apoptotic agent, the specification does not provide an indication of how the exemplified promonocytic cell line is representative of other cell lines that would have the claimed characteristics. The common attributes of the cell lines comprising the reporter gene construct are not described. Therefore, there is not a structural and functional basis provided by the prior art or the specification for one of ordinary skill in the art to envision all cell line with the claimed characteristics. According to these facts, one of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variant of the genus and is insufficient to support them.

Claims 1-34 and 70-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a promonocytic cell line that has been treated with an anti-mitotic and pro-apoptotic agent, does not reasonably provide enablement for a cell line of any other type of cell that. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation *United States v. Telectronics*, Inc., 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

1) Scope of the claims. The specification discloses that the cell line can be any prokaryotic or eukaryotic cell, but preferably are mammalian or avian cells, which is a very broad genus of cells (see paragraph 0067). The specification discloses that there are multiple classes of cell surface receptors and corresponding extracellular signals, including interferon receptors, cytokine receptors, G-coupled receptors and growth factor receptors, for example (see paragraph 0009-0024). Therefore, the claims encompass a very large genus of cells transformed with reporter gene constructs responsive to cell surface proteins and signals to regulate signal transduction activity.

2) State of the Art and Unpredictability of the art. The claimed invention is a cell line. The unpredictability in being able to make the claimed cell line is the ability to produce a cell comprising a reporter gene construct as claimed with the properties of maintaining signal transduction activity for at least about an hour and loss of activity and cellular death in no more than about 30 days. The cell lines as claimed do not provide any method steps that would produce a cell with the claimed properties. See for example claims 1 and 2, which do not recite even that the cells have been treated by any agent. It is unpredictable that any particular cell line comprising a reporter gene construct would have the property of a predictable cell death in no more than about 30 days. The specification discloses that an anti-mitotic and pro-apoptotic agent would begin to affect a cell when it begins to replicate, thereby inducing apoptosis. However, the skilled artisan would know that many cell type have different cell cycle lengths. Given the scope of the claimed cell lines that the claimed invention encompasses, it is unpredictable whether any other cell type would have the property of undergoing cell death in no more than about 30 days, 14 days or 24 hours.

3) Amount of guidance provided. The specification discloses embodiments of the claimed cell line comprising transcriptional control elements, including preferred embodiments of an interferon stimulatory response element (ISRE) wherein Type I or Type II interferon would be the extracellular signal and/or a gamma activated sequence (GAS). The specification teaches that cell lines can be irradiated with γ-radiation at a dose of about 9 grays or 6- 12 grays so that the human promonocytic cells would retain signal transduction activity for 14 days and then undergo cell death.

The specification also teaches that cell lines can be treated with vinblastine or 5-fluorourocil or cisplatin in a sufficient amount and for a sufficient time so that the signaling activity of the cells are maintained for at least about 1 hour but no more than about 30 days. The specification discloses that treated human promonocytic cell will have a shelf life of about 24 hours. The specification discloses that the time of exposure to vinblastine is variable, but also that the formulation of vinblastine is important for the desired outcome. Applicants do not provide any further specific guidance regarding how much vinblastine or cisplatin or 5-fluorourocil should be provided to any other cell type at any other concentration.

4) Working examples. In the instant case, the specification discloses a human promonocytic cell line for the claimed cell line. The cell line has been transformed with constructs comprising ISRE-SV40 operably linked to reporter gene and responsive to interferons I or II. The specification discloses treatment of cell lines with agents such as 5-fluorourcil, vinblastine or γ- radiation.

5) Nature of the invention. The invention is drawn to a cell line for signal transduction assay with a finite life span for commercial convenience.

6) Level of skill in the art. The level of skill in the art is high, but given the scope of the claim and nature of the invention, lack of guidance and working examples, state and unpredictability of the art, the skilled artisan would have to practice excessive trial and error experimentation in order to make the claimed cell lines that have the claimed properties.

Given the above analysis of the factors which the Courts have determined are critical in ascertaining whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to have practiced undue and excessive experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 12, 21, 22 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Harpold et al (US 5,436,128; cited in the IDS submitted on October 3, 2003).

This rejection is being maintained for reasons of record in the previous Office Action, mailed 4/7/2006 and for reasons outlined below.

Applicant submits that claim 1 specifically recites that the cell line maintains said signal transduction activity for at least about 1 hour but will lose said signal transduction activity and undergo cellular death in no more than 30 days. Applicant submits that the Ltk$^-$ cells, PC12 cells and COS-7 cells of Harpold, as disclosed at column 13 and exemplified in the examples, certainly do not have the property of losing signal transduction activity and undergoing cellular death in no more than 30 days at a temperature above freezing.

Applicant's arguments filed 12/5/2006 have been fully considered but they are not persuasive. As the claim is written, it recites the phrase "will lose said signal transduction activity". However, there is no limiting definition of the word "lose" in the specification that indicates that all of the activity must be lost in order to meet the claim limitation. Therefore, using the broadest interpretation of the claims, a cell that has signal transduction activity that is reduced even a small amount after at least about an hour would meet the limitation of losing signal transduction activity. Further the limitation of "at least about an hour" is a broad limitation that may encompass a time as little as 30 minutes to meet the limitation of "about an hour". Absent evidence to the contrary the

Ltk cell lines that had been transfected with the reporter construct would begin to lose signal transduction activity after at least about an hour.

Claim 1 has been amended to recite the limitation that cells must "undergo cellular death in no more than about 30 days at a temperature above freezing". Harpold et al do not specifically teach this limitation. However, other than the temperature of the claimed cell line being above freezing, no other culture conditions are specified such as change of culture medium. Absent evidence to the contrary, cells that have been transformed with a reporter gene construct and cultured for an extended time would undergo cellular death due to build up of metabolites in the culture medium. Claim 1 is drawn to a cell line and not a method or process. Absent evidence to the contrary, the cells (Ltk$^-$ cells, PC12 cells and COS-7 cells) taught by Harpold et al would meet the limitations of the claim 1.

Claims 1, 12-14, 19, 21, 22 and 25 have been rejected under 35 U.S.C. §102(b) as being anticipated by Canosi et al., *J. Immunol. Methods* 199:69-76 (1996).

This rejection is being maintained for reasons of record in the previous Office Action, mailed 4/7/2006 and for reasons outlined below. Applicant submits that the Vero cell line used by Canosi et al does not meet the property of losing signal transduction activity and undergoing cellular death in no more than 30 days at a temperature above freezing, as recited in independent claim 1.

Applicant's arguments filed 12/5/2006 have been fully considered but they are not persuasive. As discussed above, there is no limiting definition of the word "lose" in the specification that indicates that all of the activity must be lost in order to meet the claim limitation. Therefore, using the broadest interpretation of the claims, a cell that has signal transduction activity that is reduced even a small amount after at least about an hour would meet the limitation of losing signal transduction activity. Further the limitation of "at least about an hour" is a broad limitation that may encompass a time as little as 30 minutes or 2 hours to meet the limitation of "about an hour". Absent evidence to the contrary, the Vero cell line that had been transfected with the reporter construct would begin to lose signal transduction activity after at least about an hour.

As discussed above, claim 1 does not specify any other culture conditions besides temperature. Canosi et al teach that the Vero cells were grown in the wells of a 96 well culture dish. Absent evidence to the contrary, cells that have been transformed with a reporter gene construct and cultured for an extended time in small wells would undergo cellular death due to build up of metabolites in the culture medium. Claim 1 is drawn to a cell line and not a method or process. Absent evidence to the contrary, the Vero cell line taught by Canosi et al would meet the limitations of independent claim 1.

Claims 1, 12-14, 17, 19, 21 and 25 have been rejected under 35 U.S.C. §102(b) as being anticipated by Lewis, *J. Immunol. Methods* 185:9-17 (1995).

This rejection is being maintained for reasons of record in the previous Office Action, mailed 4/7/2006 and for reasons outlined below. Applicant submits that the CHO cell line and the murine Ltk$^-$ aprt$^-$ cell line used by Lewis also do not meet the property of losing signal transduction activity and undergoing cellular death in no more than 30 days at a temperature above freezing, as positively recited in claim 1.

Applicant's arguments filed 12/5/2006 have been fully considered but they are not persuasive. As discussed above, a cell that has signal transduction activity that is reduced even a small amount after at least about an hour would meet the limitation of losing signal transduction activity. Further the limitation of "at least about an hour" is a broad limitation that may encompass a time as little as 30 minutes to meet the limitation of "about an hour". Absent evidence to the contrary, the Ltk$^-$ aprt$^-$ cell line and the murine Ltk$^-$ aprt$^-$ cell line that had been transfected with the reporter construct would begin to lose signal transduction activity after at least about an hour.

As discussed above, claim 1 does not specify any other culture conditions besides temperature. Lewis teaches that the murine Ltk$^-$ aprt$^-$ cell line was grown in the wells of a 96 well culture dish. Absent evidence to the contrary, cells that have been transformed with a reporter gene construct and cultured for an extended time in small wells would undergo cellular death due to build up of metabolites in the culture medium. Claim 1 is drawn to a cell line and not a method or process. Absent evidence to the contrary, the cell lines taught would meet the limitations of independent claim 1.

Applicant's arguments, see REMARKS, filed 12/5/2006, with respect to claims 1, 12-15, 19, 21, 22 and 25-28 under 35 U.S.C. §102(b) as being anticipated by Lallemand et al have been fully considered and are persuasive. Lallemand et al teach that the U937 cell line was obtained by cotransfection of the cells with plasmids and selection of the antibiotic resistant clones after approximately 30 days of growth. The rejection of claims 1, 12-15, 19, 21, 22 and 25-28 under 35 U.S.C. §102(b) as being anticipated by Lallemand et al has been withdrawn.

Claims 1, 12, 13, 17-19, 21-23 and 25 have been rejected under 35 U.S.C. §102(b) as being anticipated by Lamb et al., U.S. Patent 5,707,803.

This rejection is being maintained for reasons of record in the previous Office Action, mailed 4/7/2006 and for reasons outlined below.

Applicant submits that there is no disclosure or teaching whatsoever in Lamb that would meet the recitation in claim 1 of losing signal transduction activity and undergoing cellular death in no more than 30 days at a temperature above freezing.

Applicant's arguments filed 12/5/2006 have been fully considered but they are not persuasive. As discussed above, a cell that has signal transduction activity that is reduced even a small amount after at least about an hour would meet the limitation of losing signal transduction activity. Further the limitation of "at least about an hour" is a broad limitation that may encompass a time as little as 30 minutes to meet the limitation of "about an hour". Absent evidence to the contrary, the HepG2 cell line that had been transfected with the reporter construct would begin to lose signal transduction activity after at least about an hour.

As discussed above, claim 1 does not specify any other culture conditions besides temperature. Absent evidence to the contrary, cells that have been transformed with a reporter gene construct and cultured for an extended time in small wells would undergo cellular death due to build up of metabolites in the culture medium. Claim 1 is drawn to a cell line and not a method or process. Absent evidence to the contrary, the cell line taught by Lamb would meet the limitations of independent claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 12, 21, 22, 24 and 25 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Harpold et al, U.S. Patent 5,436,128 in view of Button et al., *Cell Calcium* 14(9):666-671 (1993).

This rejection is being maintained for reasons of record in the previous Office Action, mailed 4/7/2006 and for reasons outlined below.

Applicant submits that the disclosures of CHO-KI, human embryonal kidney 293 and simian kidney COS cell lines do not satisfy the deficiency of Harpold's disclosure. Applicant submits that there is no suggestion or motivation in the combination of Harpold and Button for a cell line that loses signal transduction activity and undergoes cellular death in no more than about 30 days at a temperature above freezing, as positively recited in claim 1.

Applicant's arguments filed 12/5/2006 have been fully considered but they are not persuasive. The rejection of Harpold et al under USC 102 has been discussed above and maintained. Applicants' arguments do not present separate arguments regarding the Button et al reference. The Button et al reference was presented to render obvious a cell comprising aequorin as a reporter and was not meant to teach information supplied by the primary reference.

Claims 1, 12-15, 17-23 and 25-28 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Lewis in view of Lallemand and Lamb. This rejection is being maintained for reasons of record in the previous Office Action, mailed 4/7/2006 and for reasons outlined below.

Applicant submits that the deficiencies of Lewis, Lallemand and Lamb are discussed above in the anticipation rejections. Applicant submits that none of these cited and applied references alone or in combination disclose, teach, suggest or motivate one of ordinary skill in the art to arrive at the presently claimed invention.

Applicant's arguments filed 12/5/2006 have been fully considered but they are not persuasive. The rejection of Lewis et al under USC 102 has been discussed above and maintained. Applicants' arguments do not present separate arguments regarding the Lallemand and Lamb references. The Lallemand et al reference was presented to render obvious a cell comprising a reporter construct under the control of an ISRE for detection of type I interferon signaling and not meant to teach information supplied by the primary reference. The Lamb al reference was presented to render obvious a cell comprising a reporter construct under the control of a GAS element for detection of type II interferon signaling and not meant to teach information supplied by the primary reference.

Claims 29-33 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Lewis in view of Ahern, (*The Scientist* 9(15):20-27, 1995).

This rejection is being maintained for reasons of record in the previous Office Action, mailed 4/7/2006 and for reasons outlined below.

Applicant submits that Ahern's disclosure of a kit does not satisfy the deficiency in Canosi et al noted and discussed above in the anticipation rejection over Canosi. Applicant submits that the combination of Ahem and Canosi et al cannot lead one of ordinary skill in the art to a cell line (and a kit containing such a cell line) which loses its signal transduction activity and undergoes cell death in no more than 30 days at a temperature above freezing. **Applicant's arguments filed 12/5/2006 have been fully considered but they are not persuasive**. The rejection of Lewis et al under USC 102 has been discussed above and maintained. Applicants do not present separate arguments regarding the Ahern reference. The Ahern reference was presented to render obvious a kit comprising a cell line to be used for assays and not meant to teach information supplied by the primary reference.

Claims 2 and 72-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harpold et al (US 5,436,128) in view of Ausubel et al (Current Protocols in Molecular Biology, Vol. 4, pages A.3F.5-10). This is a NEW rejection.

Applicants claim a cell line in accordance with claim 1 in a frozen state wherein the cell line would maintain signal transduction activity for at least about 1 hour after being thawed but will lose the signal transduction activity and undergo cellular death in no more than 30 days at a temperature above freezing after being thawed.

The teachings of Harpold et al have been discussed in the previous Office action and in the above arguments. Harpold et al do not teach a cell line in a frozen state.

Ausubel et al teach a method of freezing cells grown in monolayer or suspension culture. Ausubel et al teach that it is desirable to freeze cells for long-term storage in order to preserve cells, avoid senescence, reduce contamination risk and minimize the effects of genetic drift (see page A.3F.6, Support Protocol 1). Ausubel et al teach that a cell suspension should be centrifuged and the supernatant (medium) should be removed and the cells should be resuspended in freezing medium (e.g. a cryopreservative), transferred into cryovials and placed in a –70°C freezer. Ausubel et al specifically teach a freezing medium comprising 10 % DMSO (see page A.3F.6, Materials).

It would be obvious to the skilled artisan at the time the invention was made to freeze the cell line as claimed in claim 1 wherein the cell line would maintain signal transduction activity for at least about 1 hours after being thawed but will lose the signal transduction activity and undergo cellular death in no more than 30 days at a temperature above freezing after being thawed as taught by Harpold et al, because Ausubel et al teach that freezing cells allows preservation of cell characteristics with reduced risk of contamination for future use. The motivation to do so would be the expected benefit of being able to use the cell line for signal transduction assay at a future time. There is a reasonable expectation of success to be able to freeze the cells taught by Harpold because the method taught by Ausubel et al is widely used in the art. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Absent evidence to the contrary the Ltk cell lines that had been transfected with the reporter construct would begin to lose signal transduction activity after at least about an hour after being thawed since losing activity can be interpreted as a small reduction in activity. Absent evidence to the contrary, cells that have been transformed with a reporter gene construct and cultured for an extended time would undergo cellular death due to build up of metabolites in the culture medium in about 30 days after being thawed. Claim 2 is drawn to a cell line and not a method or process. Therefore, Harpold et al in view of Ausubel render obvious the cell line in accordance with claim 1 in a frozen state with a cryopreservative comprising 10% DMSO (**claims 2 and 72-73**).

Claims 2 and 72-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Canosi et al, (of record) in view of Ausubel et al (Current Protocols in Molecular Biology, Vol 4, pages A.3F.5-10). This is a NEW rejection.

Applicants claim a cell line in accordance with claim 1 in a frozen state wherein the cell line would maintain signal transduction activity for at least about 1 hour after being thawed but will lose the signal transduction activity and undergo cellular death in no more than 30 days at a temperature above freezing after being thawed.

The teachings of Canosi et al have been discussed in the previous Office action and in the above arguments. Canosi et al do not teach a cell line in a frozen state with a cryopreservative.

The teaching of Ausubel et al has been detailed in the above rejection. Ausubel et al specifically teach a freezing medium comprising 10 % DMSO (see page A.3F.6, Materials).

It would be obvious to the skilled artisan at the time the invention was made to freeze the cell line as claimed in claim 1 which the cell line would maintain signal transduction activity for at least about 1 hour after being thawed but will lose the signal transduction activity and undergo cellular death in no more than 30 days at a temperature above freezing after being thawed as taught by Canosi et al because Ausubel et al teach that freezing cells allows preservation of cell characteristics with reduced risk of contamination for future use. The motivation to do so would be the expected benefit of being able to use the cell line for signal transduction assay at a future time. There is a reasonable expectation of success to be able to freeze the cells taught by Canosi et al because the method taught by Ausubel et al is widely used in the art. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Absent evidence to the contrary, the cell lines that had been transfected with the reporter construct would begin to lose signal transduction activity after at least about an hour after being thawed since losing activity can be broadly interpreted as a small reduction in activity. Absent evidence to the contrary, cells that have been transformed with a reporter gene construct and cultured for an extended time would undergo cellular death due to build up of metabolites in the culture medium in about 30 days after being thawed. Therefore, Canosi et al in view of Ausubel render obvious the cell line in accordance with claim 1 in a frozen state with a cryopreservative comprising 10 % DMSO (**claims 2 and 72-73**).

Claims 2 and 72-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lewis, (of record) in view of Ausubel et al (Current Protocols in Molecular Biology, Vol 4, pages A.3F.5-10). This is a NEW rejection.

Applicants claim a cell line in accordance with claim 1 in a frozen state wherein the cell line would maintain signal transduction activity for at least about 1 hour after being thawed but will lose the signal transduction activity and undergo cellular death in no more than 30 days at a temperature above freezing after being thawed.

The teachings of Lewis et al have been discussed in the previous Office action and in the above arguments. Lewis et al do not teach a cell line in a frozen state with a cryopreservative.

The teaching of Ausubel et al has been detailed in the above rejection. Ausubel et al specifically teach a freezing medium comprising 10 % DMSO (see page A.3F.6, Materials).

It would be obvious to the skilled artisan at the time the invention was made to freeze the cell line as claimed in claim 1 which the cell line would maintain signal transduction activity for at least about 1 hour after being thawed but will lose the signal transduction activity and undergo cellular death in no more than 30 days at a temperature above freezing after being thawed as taught by Lewis et al because Ausubel et al teach that freezing cells allows preservation of cell characteristics with reduced risk of contamination for future use. The motivation to do so would be the expected benefit of being able to use the cell line for signal transduction assay at a future time. There is a reasonable expectation of success to be able to freeze the cells taught by Lewis et al because the method taught by Ausubel et al is widely used in the art. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Absent evidence to the contrary, the Ltk$^-$ aprt$^-$ cell line and the murine Ltk$^-$ aprt$^-$ cell line that had been transfected with the reporter construct would begin to lose signal transduction activity after at least about an hour since losing activity can be broadly interpreted as a small reduction in activity. Absent evidence to the contrary, cells that have been transformed with a reporter gene construct and cultured for an extended time in small wells would undergo cellular death due to build up of metabolites in the culture medium. Claim 1 is drawn to a cell line and not a method or process. Claim 2 is drawn to a cell line and not a method or process. Therefore, Lewis in view of Ausubel et al render obvious the cell line in accordance with claim 1 in a frozen state with a cryopreservative comprising 10 % DMSO (**claims 2 and 72-73**).

Claims 2 and 72-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lamb et al (of record) in view of Ausubel et al (Current Protocols in Molecular Biology, Vol 4, pages A.3F.5-10). This is a NEW rejection.

The teachings of Lamb et al have been discussed in the previous Office action and in the above arguments. Lamb et al do not teach a cell line in a frozen state.

The teaching of Ausubel et al has been detailed in the above rejection. Ausubel et al specifically teach a freezing medium comprising 10 % DMSO (see page A.3F.6, Materials).

It would be obvious to the skilled artisan at the time the invention was made to freeze the cell line as claimed in claim 1 which the cell line would maintain signal transduction activity for at least about 1 hour after being thawed, but will lose the signal transduction activity and undergo cellular death in no more than 30 days at a temperature above freezing after being thawed as taught by Lamb et al because Ausubel et al teach that freezing cells allows preservation of cell characteristics with reduced risk of contamination for future use. The motivation to do so would be the expected benefit of being able to use the cell line for signal transduction assay at a future time. There is a reasonable expectation of success to be able to freeze the cells taught by Lamb et al because the method taught by Ausubel et al is widely used in the art. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Absent evidence to the contrary the HepG2 cell line that had been transfected with the reporter construct would begin to lose signal transduction activity after at least about an hour after being thawed. Absent evidence to the contrary, cells that have been transformed with a reporter gene construct and cultured for an extended time in small wells would undergo cellular death due to build up of metabolites in the culture medium. Absent evidence to the contrary, the cell line taught by Lamb would meet the limitations of independent claim 1. Therefore, Lamb et al in view of Ausubel renders obvious the cell line in accordance with claim 1 in a frozen state with a cryopreservative comprising 10 % DMSO (**claims 2 and 72-73**).

Claim 75 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Canosi et al (of record) in view of Ahern (of record) and further in view of Ausubel et al (Current Protocols in Molecular Biology, Vol 4, pages A.3F.5-10). This is a NEW rejection.

Applicants claim a kit comprising a testing device having a plurality of wells and a reagent containing the cell line of claim 2.

The teachings of Canosi et al have been discussed in the previous Office action and in the above arguments. Canosi et al teach that a signal transduction assay is performed in a 96 well format (i.e. a microtiter plate) (see page 71, left column, paragraph 2.6, for example). Canosi et al do not teach a cell line in a frozen state or provided in a kit.

The teaching of Ausubel et al has been detailed in the above rejection. Ausubel et al do not teach a cell line in a frozen state.

Ahern teaches that is an advantage to having a kit is that an investigator can purchase a kit rather than searching for all of the individual components of the assay and the kit provides the investigator with instructions to follow. Ahern further states, "kits accelerate the research process" (page 23).

It would be obvious to the skilled artisan at the time the invention was made to freeze the cell line taught by Canosi et al because Ausubel et al teach that freezing cells allows preservation of cell characteristics with reduced risk of contamination for future use. The motivation to do so would be the expected benefit of being able to use the cell line for signal transduction assay at a future time. There is a reasonable expectation of success to be able to freeze the cells taught by Canosi et al because the method taught by Ausubel et al is widely used in the art.

It would also have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Canosi et al to provide a kit comprising the reagents for detecting interferon levels that induce a signaling pathway because Canosi et al teaches that it is within the ordinary skill in the art to use a recombinant cells to determine the levels of IFN in a sample and because Ahern demonstrate that a kit provides an investigator with an efficient product for carrying out experiments. One would have been motivated to do so in order to receive the expected benefit, as suggested by Ahern of providing an easy, efficient and reproducible product to determine the amount of interferon in a sample. There would have been reasonable expectation of success in providing the reagents taught by Canosi et al in a kit.

Therefore, Canosi et al in view of Ahern and further in view of Ausubel render obvious the kit of claim 75.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura M. Mitchell whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Laura Mitchell, PhD
Examiner
8/20/2007

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